

Title: Angiogenically Effective Unit Dose of FGF-2 and Method of Use  
Inventor(s): Whitehouse  
Application No: 09/771,302  
Atty Dkt No: 1543.201 (5784-81A)

Fig. 1A

## Mean rFGF Plasma Concentration Versus Time Post 1C Administration

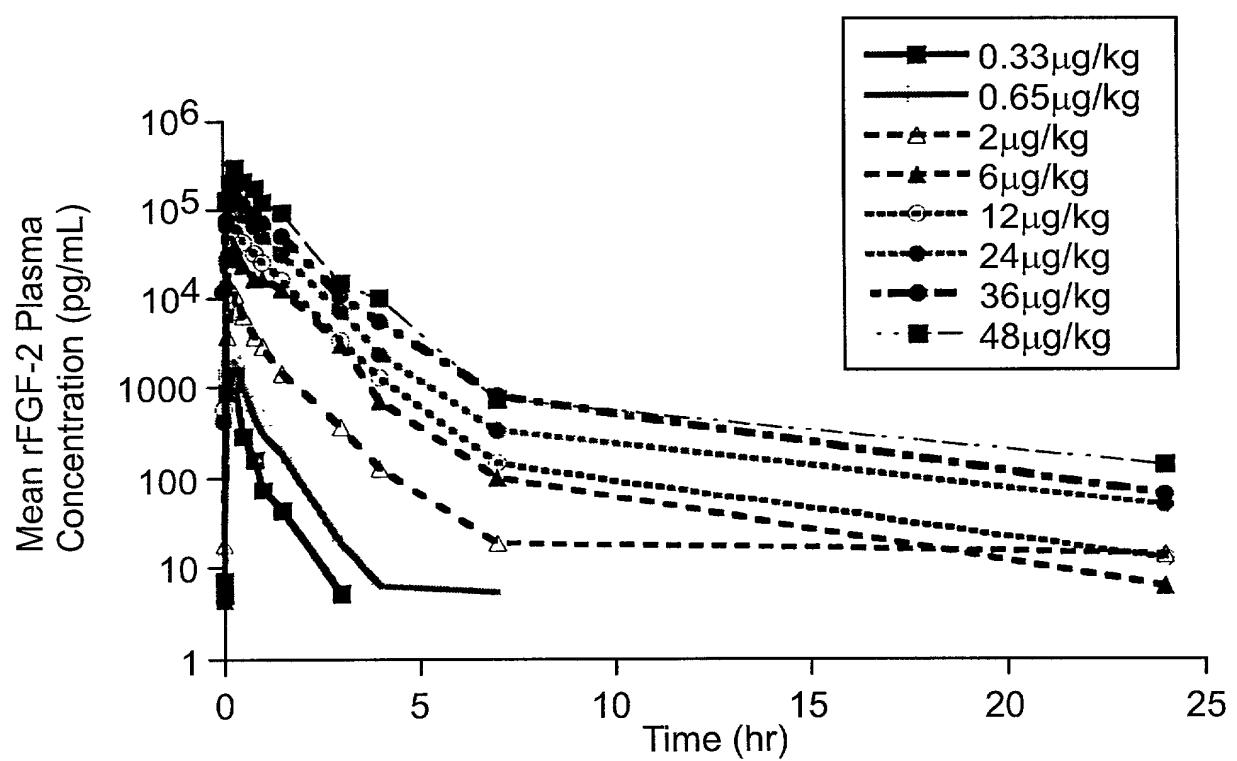
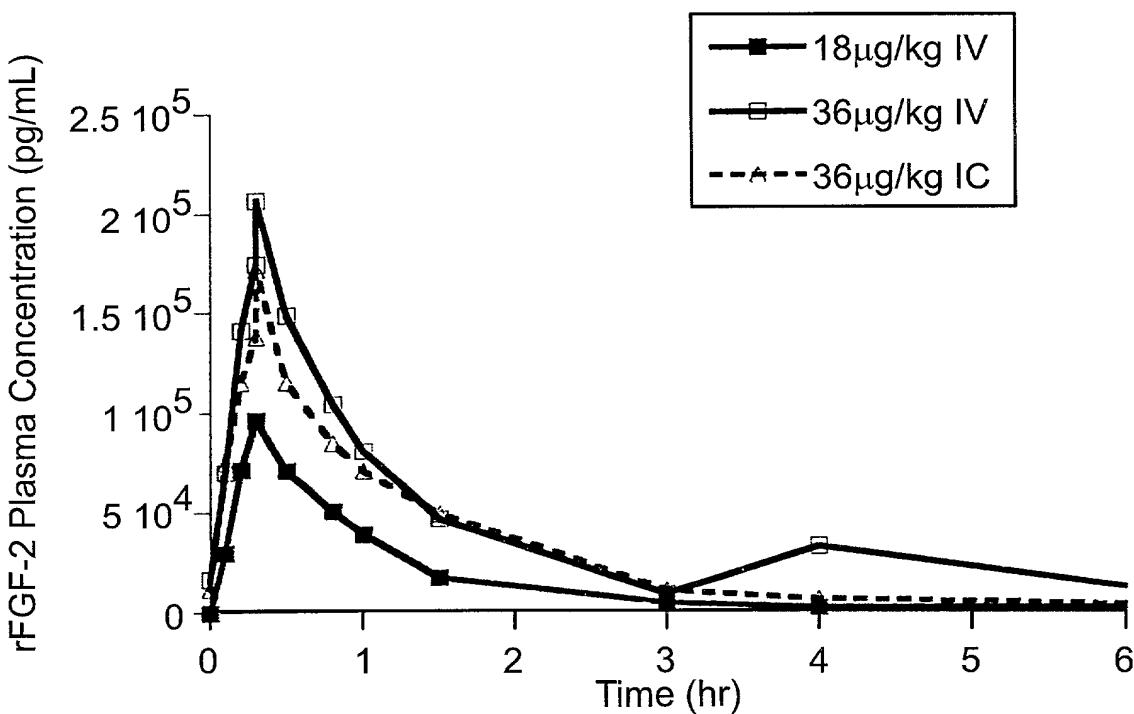


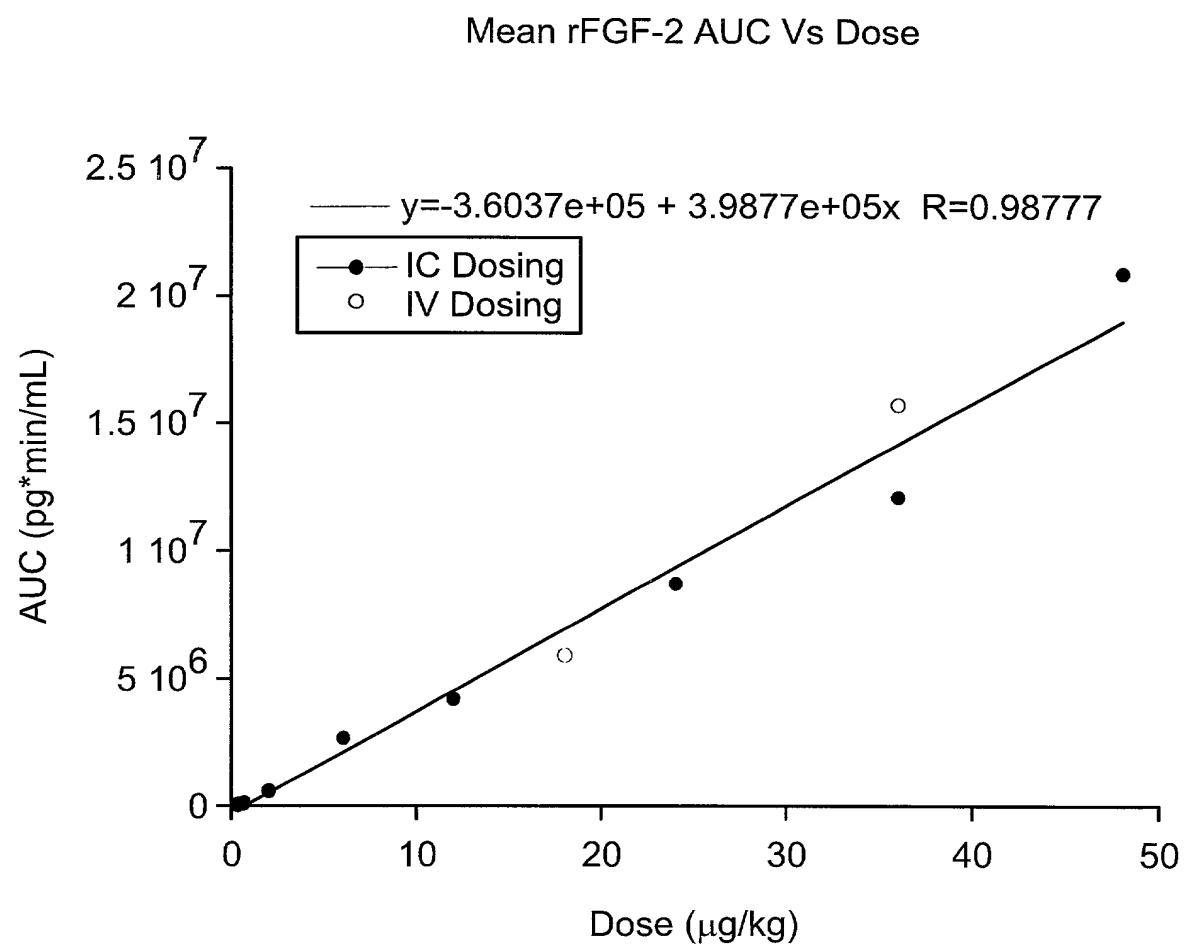
Fig. 1B

Mean rFGF-2 Plasma Concentration-Time Profiles Following IV Administration. Mean rFGF-2 Plasma Concentration Profile Following Administration of 36 $\mu$ g/kg 1C Included for Comparison.



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Fig. 2



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Fig. 3  
Individual Patient rFGF-2 Plasma Clearance Values

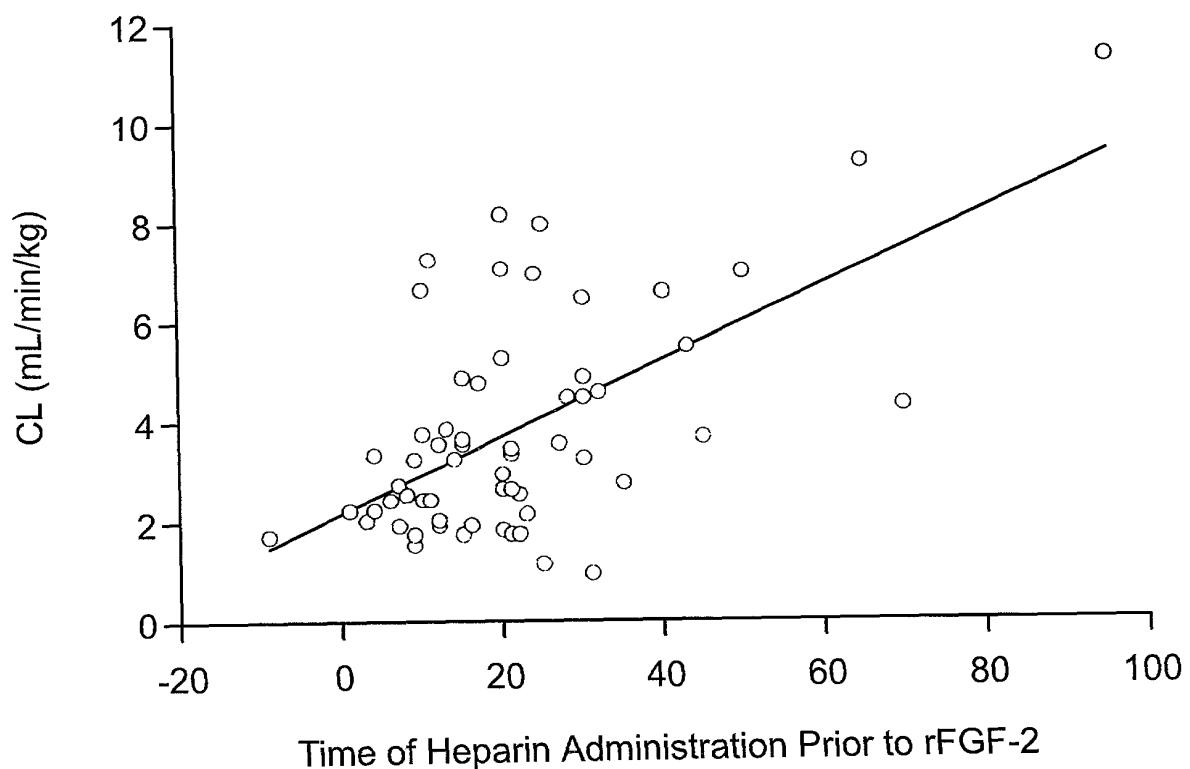
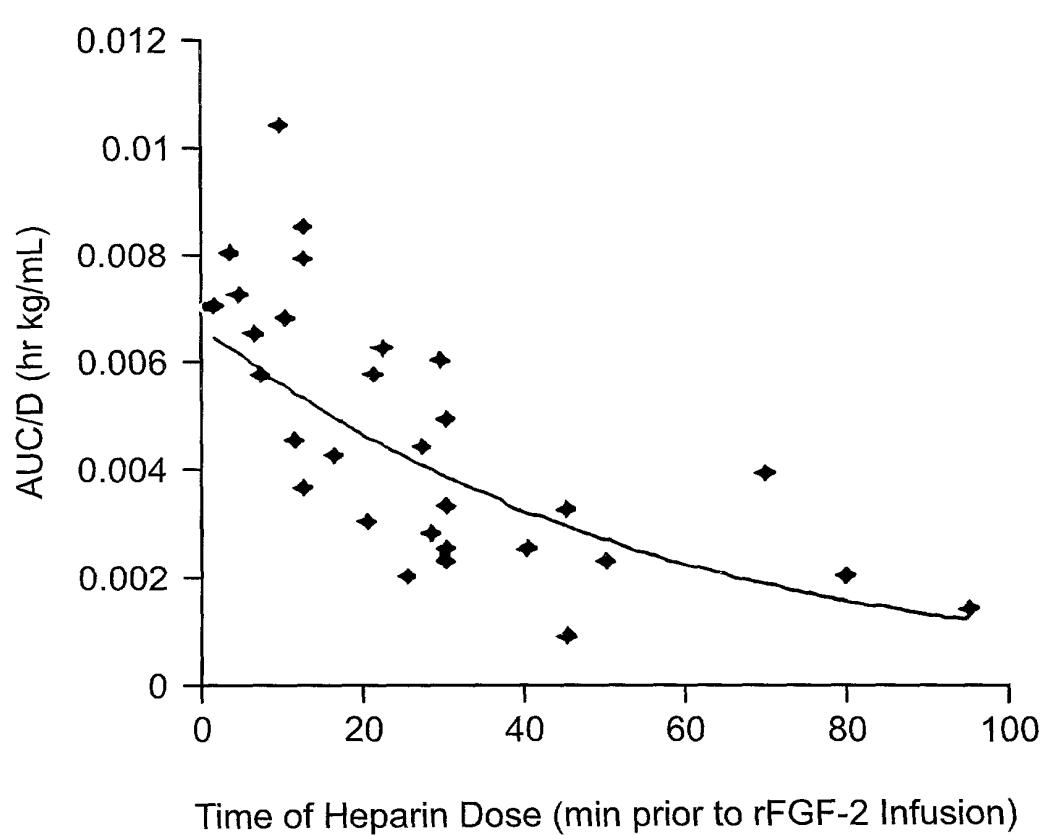


Fig. 4

Individual Patient rFGF-2 Dose-Normalized AUC  
Versus Dose in Study CS-FG001



## Fig. 5

### FIRST: Analysis Plan

- Primary Efficacy Analysis: change in ETT at 90 days for all evaluable patients by ANOVA
  - Evaluable Patients: subjects with ETT at day 90 who were not revascularized
- Secondary Analyses:
  - ANOVA of Ranks: assigns lowest rank to patients with missing data or revascularized
  - pair-wise comparisons: each dose vs placebo, any FGF vs placebo by ANOVA and ANOVA of Ranks
- Post hoc Analyses:
  - by Canadian Cardiovascular Score (CCS)
  - by angina frequency score (AFS)

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**Fig. 6**  
**FIRST: Patient Characteristics**

		rFGF-2 (μg/kg)		
	Placebo	0.3	3.0	30
Number of Subjects	86	82	84	85
Age (years)	64	63	63	62
Male sex (%)	86	84	80	86
Diabetes (%)	32	33	37	25
Dyslipidemia (%)	93	94	95	91
Hypertension (%)	77	71	68	68
Prior MI (%)	70	65	65	69
Prior CABG (%)	91	89	88	89
Prior PTCA with stent (%)	43	26	42	29
Prior PTCA w/o stent (%)	49	41	32	42
Baseline ETT time (sec)	513	527	525	514
Canadian Cardiovascular Classes II or III (%)	87	87	90	89

**Fig. 7**  
**FIRST: Patient Disposition**

		rFGF-2 (μg/kg)		
	Placebo	0.3	3.0	30
Subjects Enrolled	86	82	84	85
Safety FU: 180 days	82	76	80	83
ETT at 90/180 days	82/75	75/71	79/74	77/76
Premature Withdrawal	4	6	4	2
- Death	1	1	3	1
- Adverse Event	1	2	1	0
- Withdraw Consent	1	1	0	1
- Lost to Follow-up	0	1	0	0
- Protocol Deviation/ Violation	0	1	0	0
- Nonclassified	1	0	0	0
Revascularized Subjects Excluded from Analysis	5	5	3	6

**Fig. 8**  
**FIRST: Safety**

		rFGF-2 (μg/kg)	
	Placebo	0.3	3.0
Number of Subjects	86	82	84
All Serious Events	29 (34%)	29 (35%)	22 (26%)
Deaths	1	1	3
Carcinoma	1	0	1
Cardiac Events			
Admissions for Angina/Chest Pain	18	12	8
Cardiac Arrest	0	1	2
Myocardial Infarct	5	2	5
Revascularizations	5	5	3
Laboratory Findings			
Clearance: < 60 mL/min	4	0	1
Creatinine: ≥ 2.5 mg/dL	None	None	None
Proteinuria: > 300 mg/24 h	4	5	4
			5

Fig. 9

Change in Exercise Time  
*Primary Efficacy Analysis at Day 90: overall p = .64*

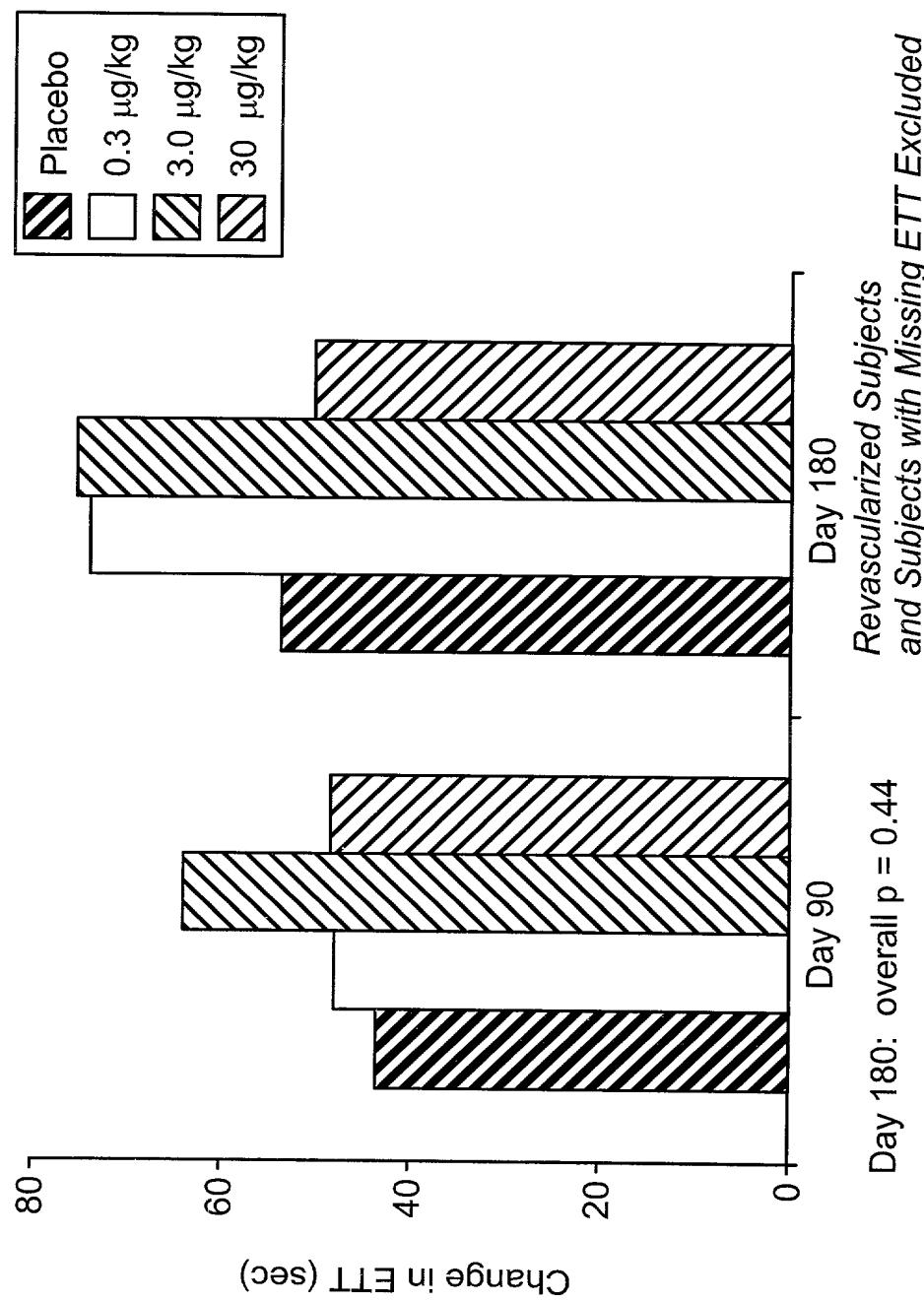


Fig. 10  
Change in Angina Frequency Score

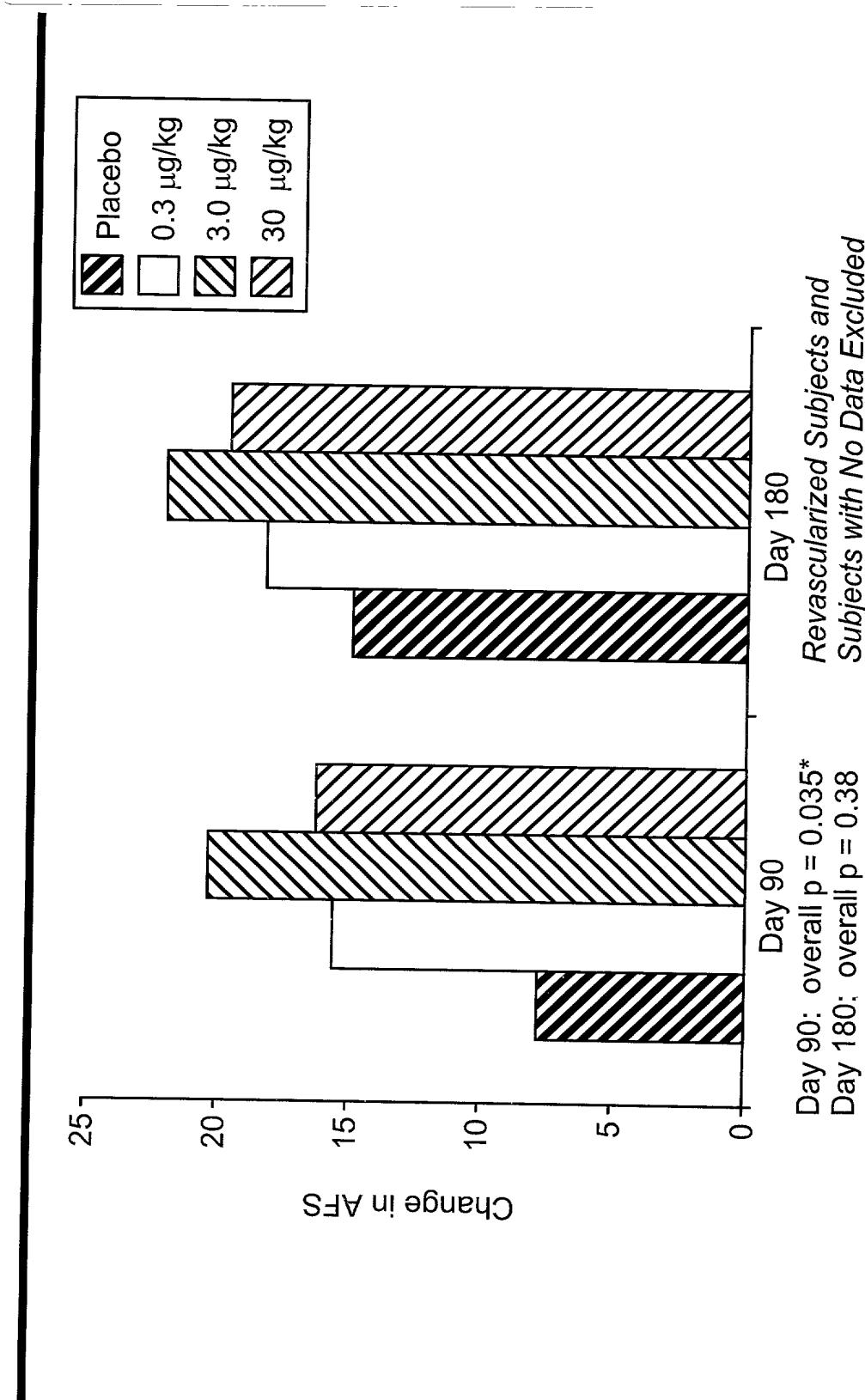


Fig. 11

Seattle Angina Questionnaire  
Change in Other Domains

- Placebo
- 0.3  $\mu$ g/kg
- 3.0  $\mu$ g/kg
- 30  $\mu$ g/kg

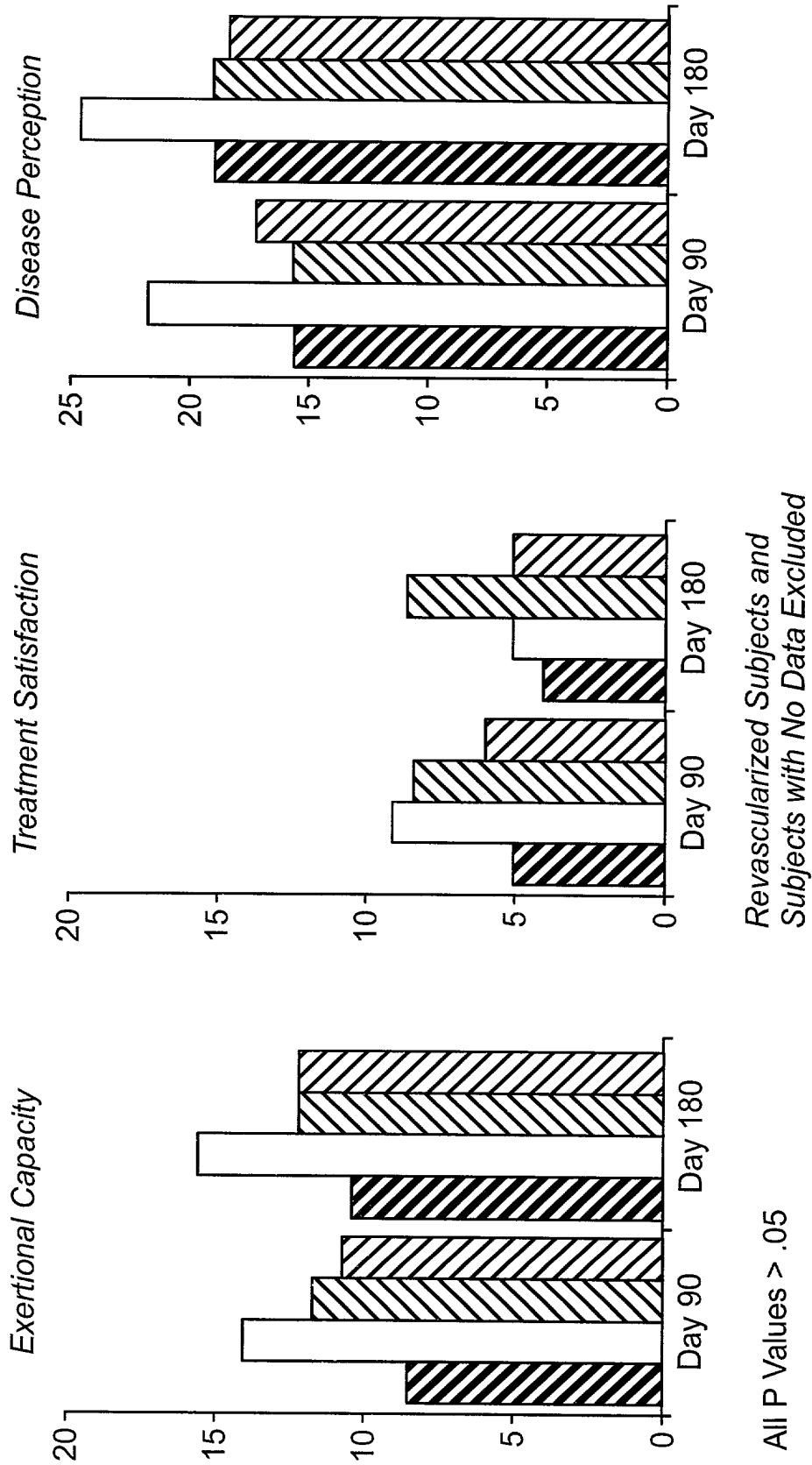


Fig. 12

Change in Short Form-36  
*Change in Physical Component Summary Score*

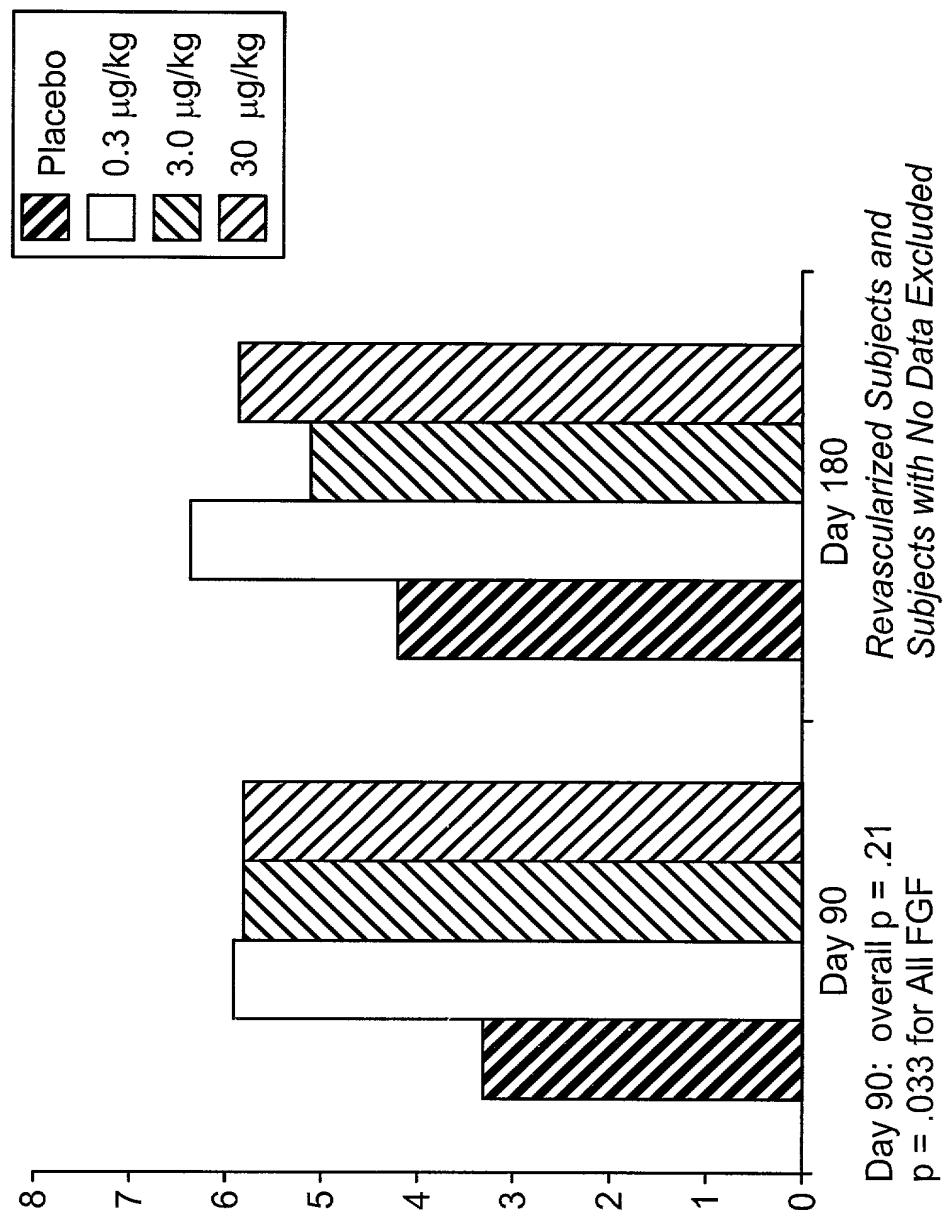


Fig. 13  
Stratified by Baseline CCS Class 3 or 4

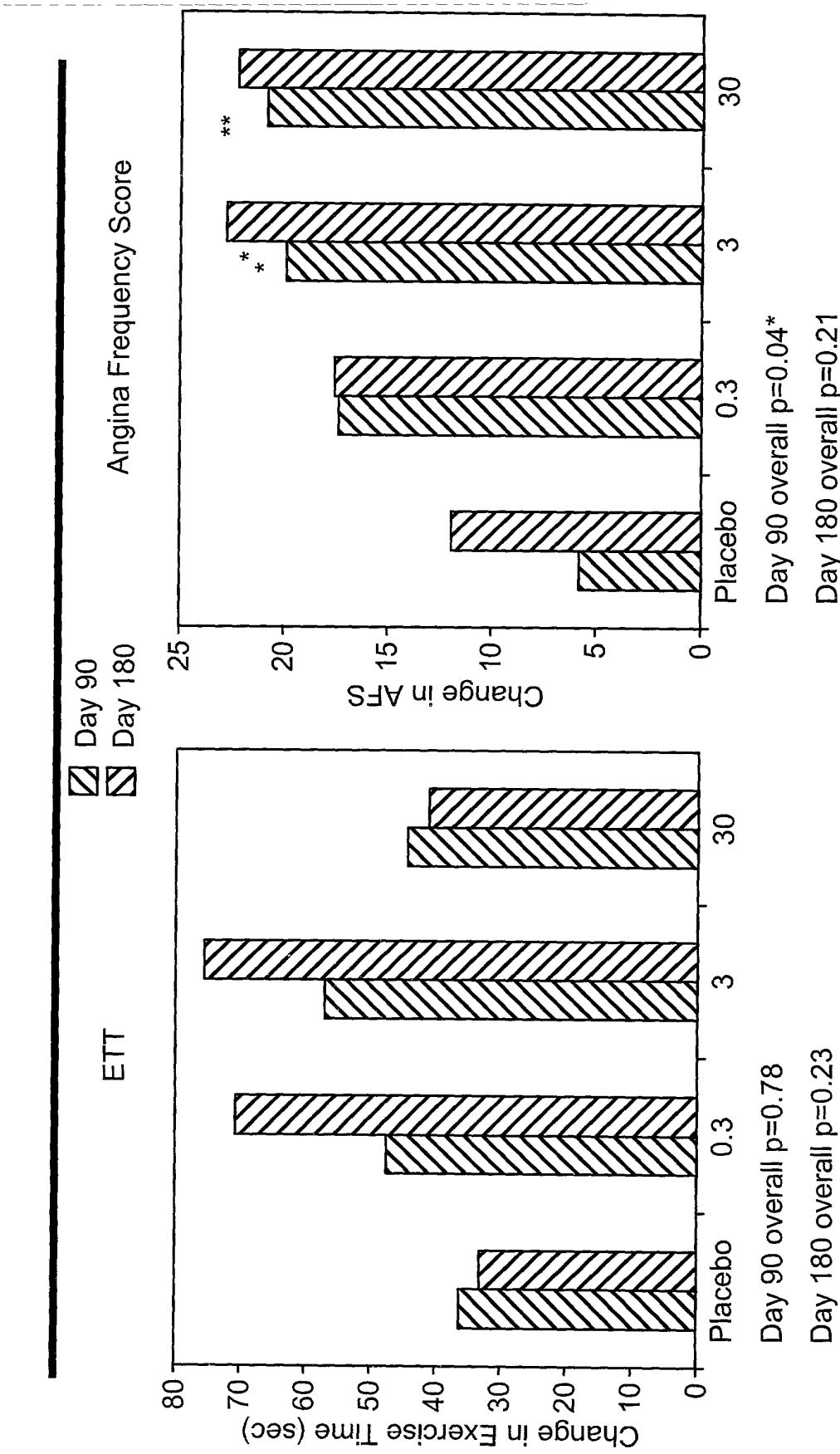


Fig. 14  
Stratified by Baseline AFS  $\leq 40$

